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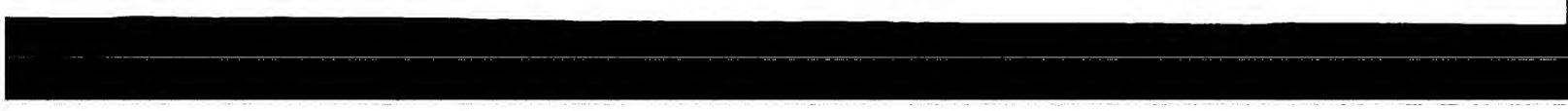
(FILE 'HOME' ENTERED AT 18:01:22 ON 25 FEB 2004)

FILE 'MEDLINE' ENTERED AT 18:01:29 ON 25 FEB 2004

L1	14453	S	PAPILLOMAVIRUS
L2	36156	S	HERPESVIRUS
L3	322	S	L1 AND L2
L4	79707	S	VACCINE
L5	8	S	L3 AND L4
L6	53714	S	ADJUVANT
L7	1	S	CCPG
L8	6330	S	CPG
L9	0	S	L3 AND L8
L10	5	S	3D-MPL
L11	5	S	"3D-MPL"
L12	40	S	QS21
L13	0	S	L3 AND L12
L14	0	S	L3 AND L8
L15	1	S	L6 AND L3
L16	64	S	L1 (P) L2
L17	1	S	L16 AND L4
L18	21	S	L8 AND L1
L19	73	S	L2 AND L8
L20	1	S	L12 AND L1



Adult
Follow-Up Studies
HIV Antibodies: BL, blood
HIV Antibodies: ME, metabolism
HIV Envelope Protein gp120: AE, adverse effects
*HIV Envelope Protein gp120: IM, immunology
HIV Envelope Protein gp120: ME, metabolism
*HIV Seronegativity: IM, immunology
*HIV-1: IM, immunology
Immunization Schedule
Lipid A: AD, administration & dosage
Lipid A: AE, adverse effects
*Lipid A: AA, analogs & derivatives
Lipid A: PD, pharmacology
Neutralization Tests
Vaccines, Synthetic: AD, administration & dosage
Vaccines, Synthetic: AE, adverse effects
*Vaccines, Synthetic: IM, immunology
CN 0 (AIDS Vaccines); 0 (Adjuvants, Immunologic); 0 (HIV Antibodies); 0 (HIV Envelope Protein gp120); 0 (Lipid A); 0 (Vaccines, Synthetic); 0 (monophosphoryl lipid A)

L11 ANSWER 5 OF 5 MEDLINE on STN
AN 1999345239 MEDLINE
DN 99345239 PubMed ID: 10418898
TI The adjuvant combination monophosphoryl lipid A and QS21 switches T cell responses induced with a soluble recombinant HIV protein from Th2 to Th1.
AU Moore A; McCarthy L; Mills K H
CS Department of Biology, National University of Ireland, Maynooth, Co. Kildare.
SO VACCINE, (1999 Jun 4) 17 (20-21) 2517-27.
Journal code: 8406899. ISSN: 0264-410X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199908
ED Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990826
AB The induction of protective immunity with recombinant vaccines is dependent on the identification of adjuvant or delivery systems that can augment immune responses, especially cellular immune responses, to soluble protein antigen. In this study we demonstrate that an adjuvant formulation comprising QS21, a purified form of saponin and 3D-monophosphoryl lipid A (MPL), a nontoxic derivative of lipopolysaccharide (LPS), enhances cellular and humoral immune responses to a recombinant HIV protein. Analysis of cytokine secretion by antigen-specific T-cells from the spleen demonstrated that QS21 augmented Th1 and Th2 responses, whereas addition of **3D-MPL** resulted in preferential induction of type 1 T-cells. Furthermore, analysis of the subclass of the IgG antibody in the serum in mice immunized with gp120 with the combined adjuvant formulation confirmed the selective activation of Th1 cells in vivo. **3D-MPL** was found to enhance B7-1 expression and IL-12 production by macrophages, which are known to be involved in the LPS-induced enhancement of Th1 responses. Thus **3D-MPL** appears to act as an adjuvant, without the toxicity associated with LPS, by controlled and selective potentiating effects on antigen presentation and T-cell activation.
CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
*AIDS Vaccines: AD, administration & dosage
AIDS Vaccines: IM, immunology

*Hepatitis B Surface Antigens: AD, administration & dosage
Hepatitis B Surface Antigens: IM, immunology
*Hepatitis B Vaccines: AD, administration & dosage
Hepatitis B Vaccines: AE, adverse effects
Hepatitis B Vaccines: IM, immunology
Middle Age

CN 0 (HLA-DQ Antigens); 0 (HLA-DQ2); 0 (Hepatitis B Surface Antigens); 0 (Hepatitis B Vaccines)

L11 ANSWER 4 OF 5 MEDLINE on STN
AN 2000113866 MEDLINE
DN 20113866 PubMed ID: 10649617
TI A phase I trial in HIV negative healthy volunteers evaluating the effect of potent adjuvants on immunogenicity of a recombinant gp120W61D derived from dual tropic R5X4 HIV-1ACH320.
AU McCormack S; Tilzey A; Carmichael A; Gotch F; Kepple J; Newberry A; Jones G; Lister S; Beddows S; Cheingsong R; Rees A; Babiker A; Banatvala J; Bruck C; Darbyshire J; Tyrrell D; Van Hoecke C; Weber J
CS Department of Virology, St Thomas' Hospital (UMDS), London, UK.
SO VACCINE, (2000 Jan 18) 18 (13) 1166-77.
Journal code: 8406899. ISSN: 0264-410X.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals; AIDS
EM 200003
ED Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000322
AB Thirty healthy HIV negative volunteers were randomised to receive 200 micrograms of rgp120W61D in either: **3D-MPL** and QS21, with an oil and water emulsion (SBAS-2) (13); or **3D-MPL** and QS21 (SBAS-1) (11); or alum (six). Immunizations were given at 0, 4 and 28 weeks and 23 (77%) participants completed the schedule. Adverse events were more frequent ($P < 0.001$) and more severe ($P < 0.001$) in the SBAS-2 group. Binding antibodies to the homologous rgp120W61D were detected after the first immunisation only in those receiving SBAS-1 and SBAS-2, were maximal after the third immunization in all three groups, and persisted to week 84 only in the novel adjuvant groups. These differences were significant ($p = 0.02$). Neutralising antibodies to TCLA-strains of HIV-1 were observed after the second immunization in all three groups, were maximal after the third immunization, but did not neutralise homologous or heterologous PBMC derived primary HIV-1 isolates. Proliferative T-cell responses to rgp120W61D were maximal after the second immunization and reached very high values in the SBAS-2 group. HIV-1 specific CD8+ MHC Class I restricted cytotoxic T-lymphocytes were not seen in a subset of participants tested at a single timepoint. SBAS-2 with rgp120W61D induced antibody titres as high as those seen in HIV infection, but the quality of the antibodies remained different in that there was no evidence of primary isolate neutralisation. Although cell-mediated immunity was enhanced by SBAS-2 in terms of lymphoproliferative responses, HIV-1 specific CD8+ cytotoxicity was not demonstrated.
CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
AIDS Vaccines: AE, adverse effects
*AIDS Vaccines: IM, immunology
Adjuvants, Immunologic: AD, administration & dosage
Adjuvants, Immunologic: AE, adverse effects
*Adjuvants, Immunologic: PD, pharmacology

Lymphocyte Activation: IM, immunology
Middle Age
Single-Blind Method
Vaccines, Combined: AE, adverse effects
Vaccines, Combined: IM, immunology
Vaccines, Combined: TU, therapeutic use
Vaccines, Synthetic: AE, adverse effects
Vaccines, Synthetic: IM, immunology
Vaccines, Synthetic: TU, therapeutic use

CN 0 (Adjuvants, Immunologic); 0 (Hepatitis B Antibodies); 0 (Hepatitis B Surface Antigens); 0 (Hepatitis B Vaccines); 0 (Vaccines, Combined); 0 (Vaccines, Synthetic)

L11 ANSWER 3 OF 5 MEDLINE on STN
AN 2002351230 MEDLINE
DN 22053742 PubMed ID: 12057618
TI Immune response of HLA DQ2 positive subjects, vaccinated with HBsAg/AS04, a hepatitis B vaccine with a novel adjuvant.
AU Desombere Isabelle; Van der Wielen Marie; Van Damme Pierre; Stoffel Michel; De Clercq Norbert; Goilav Christian; Leroux-Roels Geert
CS Centre for Vaccinology, Ghent University Hospital, De Pintelaan 185 9000, Ghent, Belgium.
SO VACCINE, (2002 Jun 7) 20 (19-20) 2597-602.
Journal code: 8406899. ISSN: 0264-410X.
CY England: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 200211
ED Entered STN: 20020704
Last Updated on STN: 20021214
Entered Medline: 20021127
AB About 5-10% of the general adult population respond inadequately to hepatitis B vaccination. The histocompatibility leucocyte antigen (HLA) DQ2, DR3 and DR7 phenotypes have been linked with non-responsiveness to hepatitis B vaccination. A first part of our study determined the prevalence of the HLA DQ2 allele in a healthy population, aged 15-50 years. We found 35% of our study population (n=1008) positive for the HLA DQ2 allele. Positive subjects for HLA DQ2 were subsequently invited to participate in a trial and were to be given either the HBsAg/AS04 hepatitis B vaccine or a licensed hepatitis B vaccine (Engerix-B).(1) Both contained 20 microg of recombinant HBsAg. The HBsAg/AS04 vaccine was administered on a 0 and 6 months schedule whilst the comparator vaccine was given according to the standard 0, 1 and 6 months schedule. The experimental vaccine was formulated on a novel adjuvant containing 3' deacylated monophosphoryl lipid A (**3D-MPL**) and alum.
A total of 230 subjects were enrolled into the vaccination study. At month 7, 99% of the subjects had a protective titre (>or=10mIU/ml) with a geometric mean titre (GMT) of 6613mIU/ml in the group receiving HBsAg/AS04 versus 97% seroprotected with a GMT of 2315mIU/ml in the other group. Both vaccines, with their respective schedule, give very high seroprotection rates (>96%). Our data suggest that HLA DQ2 positivity is not a good marker for non- or poor-responsiveness. The HBsAg/AS04 vaccine was more reactogenic mainly because of an increased local reactogenicity. Both vaccines, especially HBsAg/AS04, are highly immunogenic and well tolerated by the study subjects.
CT Check Tags: Female; Human; Male
Adolescent
Adult
*HLA-DQ Antigens: BL, blood

[redacted]

(Lipid A); 0 (monophosphoryl lipid A)

L11 ANSWER 2 OF 5 MEDLINE on STN
AN 2002640668 MEDLINE
DN 22287247 PubMed ID: 12399191
TI The immunogenicity and reactogenicity profile of a candidate hepatitis B vaccine in an adult vaccine non-responder population.
AU Jacques P; Moens G; Desombere I; Dewijngaert J; Leroux-Roels G; Wettendorff M; Thoelen S
CS Interdisciplinaire Dienst voor het Welzijn, IDEWE, Leuven, Belgium.
SO VACCINE, (2002 Nov 1) 20 (31-32) 3644-9.
Journal code: 8406899. ISSN: 0264-410X.
CY Netherlands
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 200305
ED Entered STN: 20021026
Last Updated on STN: 20030531
Entered Medline: 20030530
AB Approximately 5% of vaccinees display an inadequate response after the administration of the standard three dose hepatitis B vaccine. A new hepatitis B vaccine (HBsAg/AS04) formulated with the adjuvant AS04 which contains 3'-deacylated monophosphoryl lipid A (**3D-MPL**) and alum has been developed. AS04 enhances the immune response which may be beneficial to non-responders. In a single-blind, randomised study, we tested the immunogenicity and reactogenicity of the new vaccine with that of commercially established hepatitis B vaccine, both on a 0, 1, 6 months schedule in 20-60 years old non-responders (titre <10 m IU/ml after four doses of hepatitis B vaccine). One month after the first dose the seroprotection rate was 44% for group 1 (58 subjects) receiving the established vaccine versus 66% for group 2 receiving HBsAg/AS04 (57 subjects) (P=0.03). One month after the second dose this was 58 and 81%, respectively (P<0.005) and 1 month after the third dose this was 68 and 98%, respectively (P<0.001). One month after each dose, GMTs were 34, 56 and 111 mIU/ml for group 1 versus 123222 and 1937 mIU/ml for the HBsAg/AS04 group (P<0.05, <0.01 and 0.0001, respectively). Pain at the injection site was the most commonly reported local symptom and very few symptoms were scored as severe. In this group of adult non-responders to previous hepatitis vaccination, the HBsAg/AS04 vaccine was well tolerated and induced, at all time-points, a superior immune response compared to the licensed hepatitis B vaccine.
CT Check Tags: Comparative Study; Female; Human; Male
Adjuvants, Immunologic: AE, adverse effects
Adjuvants, Immunologic: TU, therapeutic use
Adult
*Hepatitis B: PC, prevention & control
Hepatitis B Antibodies: BI, biosynthesis
Hepatitis B Antibodies: BL, blood
Hepatitis B Surface Antigens: AE, adverse effects
Hepatitis B Surface Antigens: BL, blood
Hepatitis B Surface Antigens: IM, immunology
Hepatitis B Surface Antigens: TU, therapeutic use
*Hepatitis B Vaccines: AE, adverse effects
*Hepatitis B Vaccines: IM, immunology
Hepatitis B Vaccines: TU, therapeutic use
*Hepatitis B Virus: IM, immunology
Histocompatibility Testing
Immunity, Cellular: IM, immunology
Immunization Schedule

L11 ANSWER 1 OF 5 MEDLINE on STN
AN 2003155985 MEDLINE
DN 22559121 PubMed ID: 12674200
TI High-dose antibiotic therapy is superior to a 3-drug combination of prostanoids and lipid A derivative in protecting irradiated canines.
AU Kumar K Sree; Srinivasan V; Toles Raymond E; Miner Venita L; Jackson William E; Seed Thomas M
CS Radiation Casualty Management Team, Armed Forces Radiobiology Research Institute, Bethesda, MD 20889, USA.. kumar@afrri.usuhs.mil
SO JOURNAL OF RADIATION RESEARCH, (2002 Dec) 43 (4) 361-70.
Journal code: 0376611. ISSN: 0449-3060.
CY Japan
DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200304
ED Entered STN: 20030404
Last Updated on STN: 20030426
Entered Medline: 20030425
AB There is an urgent need to develop non-toxic radioprotectors. We tested the efficacy of a 3-drug combination (3-DC) of iloprost, misoprostol, and **3D-MPL** (3-deacylated monophosphoryl lipid A) and the effects of postirradiation clinical support with high doses of antibiotics and blood transfusion. Canines were given 3-DC or the vehicle and exposed to 3.4 Gy or 4.1 Gy of 60Co radiation. Canines irradiated at 4.1 Gy were also given clinical support, which consisted of blood transfusion and antibiotics (gentamicin, and cefoxitin or cephalexin). Peripheral blood cell profile and 60-day survival were used as indices of protection. At 3.4 Gy, 3-DC- or vehicle-treated canines without postirradiation clinical support survived only for 10 to 12 days. Fifty percent of the canines treated with 3-DC or vehicle and provided postirradiation clinical support survived 4.1-Gy irradiation. Survival of canines treated with vehicle before irradiation significantly correlated with postirradiation antibiotic treatments, but not with blood transfusion. The recovery profile of peripheral blood cells in 4.1 Gy-irradiated canines treated with vehicle and antibiotics was better than drug-treated canines. These results indicate that therapy with high doses of intramuscular aminoglycoside antibiotic (gentamicin) and an oral cephalosporin (cephalexin) enhanced survival of irradiated canines. Although blood transfusion correlated with survival of 3-DC treated canines, there were no additional survivors with 3-DC treated canines than the controls.
CT Check Tags: Animal; Comparative Study
*Antibiotics, Combined: TU, therapeutic use
Blood Transfusion
*Cefoxitin: TU, therapeutic use
*Cephalexin: TU, therapeutic use
Dogs
Drug Combinations
*Gentamicins: TU, therapeutic use
*Iloprost: TU, therapeutic use
Lethal Dose 50
Leukocyte Count
*Lipid A: AA, analogs & derivatives
*Lipid A: PD, pharmacology
*Misoprostol: TU, therapeutic use
*Radiation Injuries: DT, drug therapy
Survival Analysis
RN 15686-71-2 (Cephalexin); 35607-66-0 (Cefoxitin); 59122-46-2 (Misoprostol); 78919-13-8 (Iloprost)
CN 0 (Antibiotics, Combined); 0 (Drug Combinations); 0 (Gentamicins); 0

*Adjuvants, Immunologic: AD, administration & dosage
Antigens, CD80:

[redacted]

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1: Wettendorff M. Related Articles, Links

Therapeutic vaccination.
Virus Res. 2002 Jan 30;82(1-2):133-40. Review. No abstract available.
PMID: 11885940 [PubMed - indexed for MEDLINE]

2: Salker R, Howell DR, Moore MC, Kitchen AD. Related Articles, Links

Early acute hepatitis B infection and hepatitis B vaccination in blood donors.
Transfus Med. 2001 Dec;11(6):463. No abstract available.
PMID: 11851946 [PubMed - indexed for MEDLINE]

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Overview: past and future of immunologic intervention in the pathogenesis, prophylaxis and therapeusis of hepatitis B.
J Gastroenterol Hepatol. 2002 Dec;17 Suppl:S449-51. Review. No abstract available.
PMID: 12534776 [PubMed - indexed for MEDLINE]

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Hepatitis B: progress in the last decade.
Semin Liver Dis. 2003 Feb;23(1):1-4. No abstract available.
PMID: 12616446 [PubMed - indexed for MEDLINE]

5: Madalinski K. Related Articles, Links

[Persistence of immunity after hepatitis B vaccination]
Przegl Epidemiol. 2002;56(4):605-13. Review. Polish.
PMID: 12666586 [PubMed - indexed for MEDLINE]

6: [No authors listed] Related Articles, Links

Twinrix: A combination hepatitis A and B vaccine.
Med Lett Drugs Ther. 2001 Aug 6;43(1110):67-8. No abstract available.
PMID: 11490322 [PubMed - indexed for MEDLINE]

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Travel medicine: key to improved adult vaccination against Hepatitis A and B.
J Travel Med. 2001 Jan;8 Suppl 1:S1-2. No abstract available.
PMID: 11182610 [PubMed - indexed for MEDLINE]

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Prospects for active immunotherapies for hepatitis B virus chronic carriers.
Res Virol. 1997 Mar-Apr;148(2):95-9. No abstract available.
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Response to hepatitis B vaccination in a mental handicap hospital.
J Intellect Disabil Res. 1996 Oct;40 (Pt 5):485-6. No abstract available.
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The beneficial effect of a journalist's death on organ transplantation and hepatitis B vaccination.
Nephrol Dial Transplant. 2000 May;15(5):742-3. No abstract available.
PMID: 10809835 [PubMed - indexed for MEDLINE]

☐ **11:** Meyerhoff AS, Greenberg DP. Related Articles, Links

2-dose hepatitis vaccination versus 3-dose regimen.
Pediatrics. 2002 Jun;109(6):1183-4; author reply 1183-4. No abstract available.
PMID: 12042564 [PubMed - indexed for MEDLINE]

☐ **12:** Feiterna-Sperling C. Related Articles, Links

[Hepatitis B vaccination and immunoprotection of pediatric nurses]
Kinderkrankenschwester. 1994 Jun;13(6):200-1. German. No abstract available.
PMID: 8011472 [PubMed - indexed for MEDLINE]

☐ **13:** Perera J, Perera B, Gamage S. Related Articles, Links

Seroconversion after hepatitis B vaccination in healthy young adults, and the effect of a booster dose.
Ceylon Med J. 2002 Mar;47(1):6-8.
PMID: 12001615 [PubMed - indexed for MEDLINE]

☐ **14:** Koff RS. Related Articles, Links

Hepatitis A, hepatitis B, and combination hepatitis vaccines for immunoprophylaxis: an update.
Dig Dis Sci. 2002 Jun;47(6):1183-94. Review.
PMID: 12064790 [PubMed - indexed for MEDLINE]

☐ **15:** Meng J, Yue Y, Zhang S. Related Articles, Links

[Effect of intrauterine hepatitis B virus infection on hepatitis B vaccine inoculation in newborns]
Zhonghua Fu Chan Ke Za Zhi. 2002 Mar;37(3):136-8. Chinese.
PMID: 11953078 [PubMed - indexed for MEDLINE]

☐ **16:** Rich JD, Ching CG, Lally MA, Gaitanis MM, Schwartzapfel B, Charuvastra A, Beckwith CG, Flanigan TP. Related Articles, Links

A review of the case for hepatitis B vaccination of high-risk adults.
Am J Med. 2003 Mar;114(4):316-8. Review.
PMID: 12681460 [PubMed - indexed for MEDLINE]

☐ **17:** Bosnak M, Dikici B, Bosnak V, Haspolat K. Related Articles, Links

Accelerated hepatitis B vaccination schedule in childhood.
Pediatr Int. 2002 Dec;44(6):663-5.
PMID: 12421266 [PubMed - indexed for MEDLINE]

☐ **18:** Yuen MF, Lai CL. Related Articles, Links

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PMID: 11446332 [PubMed - indexed for MEDLINE]

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☐ **20:** Emir S, Buyukpamuk M, Akyuz C, Kutluk T, Guler E, Caglar K. Related Articles, Links

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Pediatr Hematol Oncol. 2002 Jun;19(4):227-33.
PMID: 12051588 [PubMed - indexed for MEDLINE]

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